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10/696,572	10/30/2003	Masataka Andoh	016778-0470	5923

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FOLEY AND LARDNER LLP  
SUITE 500  
3000 K STREET NW  
WASHINGTON, DC 20007

EXAMINER

NEGIN, RUSSELL SCOTT

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 09/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/696,572

Applicant(s)

ANDOH ET AL.

Examiner

Russell S. Negin

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 20 June 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-34 is/are pending in the application.
- 4a) Of the above claim(s) 4, 16, 29, 30 and 32-34 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3, 5-15, 17-28, 31 is/are rejected.
- 7) ☒ Claim(s) 12 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 7/1/04.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's election of Species A in the reply filed on 20 June 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 4, 16, 29, 30, and 32-34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 20 June 2006.

Accordingly, claims 1-3, 5-15, 17-28, and 31 will be examined on the merits in this Office action.

### ***Specification***

The disclosure is objected to because of the following informalities: Page 2, line 1 of the specification states, "cDNA are d nsle fix d as a r fer nc probe in an array on a slide glass."

Appropriate correction is required.

### ***Claim Objections***

Claim 12 is objected to because of the following informalities:

In line 5 of claim 12, the word "the" is spelled incorrectly as "teh."

Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5-15, 17-28, and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The preambles to claims 1, 13, and 26 contain the phrase, "correcting global and local distortions of microarray data more precisely..." However, it is indefinite and ambiguous to what the more precise determination is compared.

Moreover, claims 1, 13, and 26 also contain the phrase, "considering flag information indicating a removal of background noise and reliability of each spot..." It is unclear and ambiguous as to how this flag information is related to the input device.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 6, 13, 14, 26, and 27 rejected under 35 U.S.C. 102(b) as being anticipated by Yang et al. [Nucleic Acids Research, February 2002, vol 30, e15, 10 pages].

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Claims 1, 2, 6, 13, 14, 26, and 27 state:

1. A cDNA microarray data correction system for correcting global and local distortions of microarray data more precisely and correcting measurement errors caused by a difference in sensitivity between fluorescent dyes, comprising: an input device for inputting previously-adjusted gene expression intensity data, considering flag information indicating a removal of background noise and reliability of each spot; a data standardization means for standardizing the gene expression intensity data by using grid-by-grid order statistics for the input gene expression intensity data and for transmitting the standardized gene expression intensity data; first correction means for estimating a distortion depending on a spot position on grid coordinates for the standardized gene expression intensity data by a nonparametric smoothing method and for transmitting first corrected gene expression intensity data whose distortion has been corrected; and second correction means for performing an S-D transformation for the first corrected gene expression intensity data, for estimating a potential distortion caused by a difference in sensitivity between the fluorescent dyes in the gene expression intensity data by the nonparametric smoothing method, and for transmitting second corrected gene expression intensity data whose distortion caused by the difference in sensitivity between the fluorescent dyes has been corrected; and an output device for outputting the second corrected gene expression intensity data.

2. The cDNA microarray data correction system according to claim 1, further comprising S-D transformation means for quantifying the distortion of the gene expression intensity data in an arbitrary stage and for visualizing it on an S-D plot.

6. The cDNA microarray data correction system according to claim 1, wherein the standardized gene expression intensity data is represented by a sum of a true gene intensity and a distortion depending on the spot position.

13. A cDNA microarray data correction method of correcting global and local distortions of microarray data more precisely and correcting measurement errors caused by a difference in sensitivity between fluorescent dyes, comprising the steps of: inputting previously-adjusted gene expression intensity data, considering flag information indicating a removal of background noise and reliability of each spot; standardizing the gene expression intensity data by using grid-by-grid order statistics for the input gene expression intensity data on condition that most genes are in a non-expression state; outputting the standardized gene expression intensity data; estimating a distortion depending on the spot position on grid coordinates for the standardized gene expression intensity data by a nonparametric smoothing method and correcting the data distortion depending on the spot position; outputting the first corrected gene expression intensity data whose distortion depending on the spot position has been corrected; performing an S-D transformation for the first corrected gene expression intensity data, estimating a potential distortion caused by a difference in sensitivity between the fluorescent dyes in the gene expression intensity data by the nonparametric smoothing

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method, and correcting the distortion caused by the difference in sensitivity between the fluorescent dyes; and outputting the second corrected gene expression intensity data whose distortion caused by the difference in sensitivity between the fluorescent dyes has been corrected.

14. The cDNA microarray data correction method according to claim 13, further comprising a step of quantifying the distortion of the gene expression intensity data in an arbitrary stage and visualizing it on an S-D plot.

26. A cDNA microarray data correction program for use in correcting global and local distortions of microarray data more precisely and correcting measurement errors caused by a difference in sensitivity between fluorescent dyes with a computer to execute the steps of: inputting previously-adjusted gene expression intensity data, considering flag information indicating a removal of background noise and reliability of each spot; standardizing the gene expression intensity data by using grid-by-grid order statistics for the input gene expression intensity data on condition that most genes are in a non-expression state; outputting the standardized gene expression intensity data; estimating a distortion depending on the spot position on grid coordinates for the standardized gene expression intensity data by a nonparametric smoothing method and correcting the data distortion depending on the spot position; outputting the first corrected gene expression intensity data whose distortion depending on the spot position has been corrected; performing an S-D transformation for the first corrected gene expression intensity data, estimating a potential distortion caused by a difference in sensitivity between the fluorescent dyes in the gene expression intensity data by the nonparametric smoothing method, and correcting the distortion caused by the difference in sensitivity between the fluorescent dyes; and outputting the second corrected gene expression intensity data whose distortion caused by the difference in sensitivity between the fluorescent dyes has been corrected.

27. A computer-readable memory medium containing a cDNA microarray data correction program for use in correcting global and local distortions of microarray data more precisely and correcting measurement errors caused by a difference in sensitivity between fluorescent dyes with a computer to execute the steps of: inputting previously-adjusted gene expression intensity data, considering flag information indicating a removal of background noise and reliability of each spot; standardizing the gene expression intensity data by using grid-by-grid order statistics for the input gene expression intensity data on condition that most genes are in a non-expression state; outputting the standardized gene expression intensity data; estimating a distortion depending on the spot position on grid coordinates for the standardized gene expression intensity data by a nonparametric smoothing method and correcting the data distortion depending on the spot position; outputting the first corrected gene expression intensity data whose distortion depending on the spot position has been corrected; performing an S-D transformation for the first corrected gene expression intensity data, estimating a potential distortion caused by a difference in sensitivity between the

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fluorescent dyes in the gene expression intensity data by the nonparametric smoothing method, and correcting the distortion caused by the difference in sensitivity between the fluorescent dyes; and outputting the second corrected gene expression intensity data whose distortion caused by the difference in sensitivity between the fluorescent dyes has been corrected.

The reference article of Yang et al, entitled, "Normalization for cDNA microarray data: a robust composite method addressing single and multiple slide systematic variation," explains multiple methods of microarray data correction.

In page 2, the section entitled "Image Processing" (middle of column 2 of Yang) states:

"Each hybridization produced a pair of 16-bit images, which were processed using the software package spot... The main quantities of interest produces by the image analysis methods (segmentation and background correction) are the  $(R,G)$  fluorescence intensity pairs for each gene on each array (where  $R$  = red for Cy5 and  $G$  = green for Cy3). Note that we have the spotted DNA sequences 'genes', whether they correspond to actual genes, ESTs or DNA sequences from other sources."

The "Image Processing" section is followed by several normalization sections from standardizing the data using MA plots. One normalization method for standardization is global normalization while the second method is intensity-dependent normalization. A third method is presented which uses "Within-print" normalization.

The final step of the statistical method is the "Scale normalization" described at the top of the first column of page 3. Yang et al state:

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"Starting from data which have been location normalized as just described , we suppose that the log ratios from the  $i$ th print tip group follow a normal distribution with mean zero and variance... "

Yang et al. continue to describe an MA plot based on the sensitivities between the dyes, which is equivalent to the definition of the applicant from an S-D transformation, as stated by Yang et al. on page 6, lines 4-19:

"An S-D plot-based correction unit for a third process performs an S-D transformation, which is a variation of on MA transformation... for the gene expression intensity data corrected up to the second process, estimates a potential distortion caused by the difference in sensitivity between the fluorescent dyes in the gene expression intensity data..." This "Scale Normalization" method of Yang et al fits this description of an S-D plot.

Figures 1-4 of Yang et al on pages 4-6 illustrate the outputs at several stages of normalization as claimed in the instant set of claims.

The last paragraph of page 9 states:

"The strengths and weaknesses of the normalization techniques and control samples discussed in this paper are summarized in Table 1. Finally, the methods described in the article are implemented in the package R (17), SMA (Statistics for Microarray Analysis), which may be downloaded from <http://www.R-project.org>. Supplemental analyses, figures and databases are available at <http://www.stat.berkeley.edu/users/terry/zarray/Html/index.html>.



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**Conclusion**

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, Ph.D., whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Andrew Wang, Supervisory Patent Examiner, can be reached at (571) 272-0811.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Yolanda Chadwick, whose telephone number is (571) 272-0514.

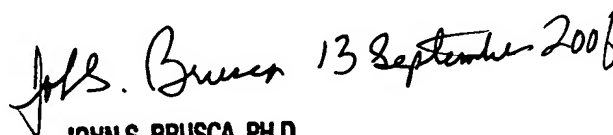
Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RSN

12 September 2006



12 Sept 2006

  
JOHN S. BRUSCA, PH.D.  
PRIMARY EXAMINER